UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/416,779	10/13/1999	FRANCO P. PREPARATA	BUV-003.01	6623

25181 7590 03/11/2002

FOLEY, HOAG & ELIOT, LLP
PATENT GROUP
ONE POST OFFICE SQUARE
BOSTON, MA 02109

EXAMINER
ZEMAN, MARY K

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 03/11/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/416,779	PREPARATA ET AL.	
	Examiner	Art Unit	
	Mary K Zeman	1631	

-- Th MAILING DATE of this communication app ars on th cover sheet with th correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 August 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6-12 and 20-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6-12 and 20-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☒ The proposed drawing correction filed on *27 August 2001* is: a)☒ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-4, 6-12 and 20-30 are pending in this application. Claims 20-30 are newly added. Claim 5 has been canceled.

The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Misnumbered claims 13-23 have been renumbered 20-30.

Applicant's arguments filed 8/27/01 have been fully considered but they are not completely persuasive. Any rejections not repeated below has been withdrawn.

The proposed drawing correction and/or the proposed substitute sheets of drawings, filed on 8/27/01 have been approved by the examiner. A proper drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The correction to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4, 6 and 20-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 90/04652, in view of Loakes et al. (1995). *This is a new grounds of rejection necessitated by Applicant's amendments to the claims.*

The claims are directed to oligonucleotide probes, or sets of probes, wherein the probes comprise universal nucleotides and designate nucleotides (or nucleotide analogs) in patterns, some of those patterns being iterative patterns.

WO 90/04652 discloses sets of oligonucleotides or probes which use "degeneracy reducing" analogs of nucleotides in order to reduce the number of oligonucleotides required to sequence large stretches of DNA. Formula II, page 4, meets the pattern limitations of claim 1, claim 20 and claim 30: The formula comprises a first string of degeneracy reducing nucleotides (I/C I/C) followed by a first segment of a designate nucleotide ("A") followed a second string of degeneracy reducing nucleotides (I/C I/C) followed by a second segment of a designate nucleotide ("A"). This formula further comprises two designate nucleotides at its 3' end, ("AA"). Sets of probes having varying patterns of fixed and degeneracy reducing nucleotides can be prepared (page 5-6, 7-9, Figure 1). Claim 4 does not require this particular pattern, but simply requires an iterative pattern, and is also met by this Formula.

The degeneracy reducing nucleotides of WO 90/04652 are not the same as the universal nucleotides.

Loakes et al. (Nucleic Acids Research 1995, Vol. 23, No. 13, pages 2361-2366; PTO-1449 Reference AI) disclose universal nucleotides such as 3-nitropyrrole and 5-nitroindole, and their usefulness in oligonucleotides to be hybridized to a target sequence. Loakes et al. disclose oligonucleotides and sets of oligonucleotides that comprise both designate and universal nucleotides in various iterative patterns, (Table 1) and assess their ability to hybridize to a target sequence. The universal nucleotides within the oligonucleotide were able to stack with the target sequence sufficiently to permit hybridization of the oligonucleotide to the target, and subsequently to prime PCR or sequencing reactions. This would indicate that such substitutions

of universal nucleotides within an oligonucleotide does not substantially interfere with the ability of the oligonucleotide to hybridize to its target sequence.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have used the universal nucleotides of Loakes et al. as the degeneracy reducing nucleotides in the oligonucleotides of WO 90/04652. Universal nucleotides are able to bind any natural nucleotide in a sequence, therefore reducing the degeneracy required in the set of probes even farther than was possible by the disclosure of WO 90/04652. One of skill in the art would have been motivated to select universal nucleotides such as those disclosed by Loakes et al., in view of their universal pairing, and their limited interference in the hybridization of an oligonucleotide with its target sequence. These are highly desirable qualities when preparing sets of probes to sequence large segments of DNA as it reduces the number of probes that actually are required to be synthesized by a great factor.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Claims 7-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 90/04652 in view of Loakes et al. as applied to claims 1-4, 6 and 20-30 above, and further in view of Chetverin et al.. *This is a new grounds of rejection necessitated by Applicant's amendments to the claims.*

Claims 7-12 add the limitation that the probes be displayed on a solid support, or sequencing chip. Claims 7-12 do not set forth any particular iterative pattern.

As set forth above, WO 90/04652 discloses sets of oligonucleotides or probes which use "degeneracy reducing" analogs of nucleotides in order to reduce the number of oligonucleotides required to sequence large stretches of DNA. Formula II, page 4, is an iterative pattern: The formula comprises a first string of degeneracy reducing nucleotides (I/C I/C) followed by a first segment of a designate nucleotide ("A") followed a second string of degeneracy reducing nucleotides (I/C I/C) followed by a second segment of a designate nucleotide ("A"). This

formula further comprises two designate nucleotides at its 3' end, ("AA"). Sets of probes having varying patterns of fixed and degeneracy reducing nucleotides can be prepared (page 5-6, 7-9, Figure 1). The degeneracy reducing nucleotides of WO 90/04652 are not the same as the universal nucleotides. WO 90/04652 does not set forth that the oligonucleotides are disposed on a solid support or sequencing chip.

Loakes et al. (Nucleic Acids Research 1995, Vol. 23, No. 13, pages 2361-2366; PTO-1449 Reference AI) disclose universal nucleotides such as 3-nitropyrrole and 5-nitroindole, and their usefulness in oligonucleotides for hybridization to a target sequence. Loakes et al. disclose oligonucleotides and sets of oligonucleotides that comprise both designate and universal nucleotides in various iterative patterns, (Table 1) and assess their ability to hybridize to a target sequence. The universal nucleotides within the oligonucleotide were able to stack with the target sequence sufficiently to permit hybridization of the oligonucleotide to the target, and subsequently to prime PCR or sequencing reactions. This would indicate that such substitutions of universal nucleotides within an oligonucleotide does not substantially interfere with the ability of the oligonucleotide to hybridize to its target sequence. Loakes et al. do not set forth that the oligonucleotides are disposed on a solid support or sequencing chip.

Chetverin et al. (Bio/Technology 1994, Vol. 12, pages 1093-1099; PTO-1449 Reference AF) disclose the great advantages to linking sets of oligonucleotide probes to solid supports. These oligonucleotide arrays have great use in the sequencing of genomic DNA or other large target sequences as cloning and manual sequencing of the genome is not required.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have used the universal nucleotides of Loakes et al. as the degeneracy reducing nucleotides in the oligonucleotides of WO 90/04652, and to further link the oligonucleotides to a solid support such as a sequencing chip as reviewed by Chetverin et al.. Universal nucleotides are able to bind any natural nucleotide in a sequence, therefore reducing the degeneracy required in the set of probes even farther than was possible by the disclosure of WO 90/04652. This allows for fewer numbers of oligonucleotides required to be linked to the array for the sequencing of large genomes. One of skill in the art would have been motivated to select universal nucleotides such as those disclosed by Loakes et al., in view of their universal pairing, and their limited interference in the hybridization of an oligonucleotide with its target sequence.

These are highly desirable qualities when preparing sets of probes to sequence large segments of DNA using sequencing chips as it reduces the number of probes that actually are required to be synthesized by a great factor, and reduces the complexity of the analysis and reconstruction of the sequence.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary K Zeman whose telephone number is (703) 305-7133. The examiner can generally be reached between the hours of 7:00 am and 1:00 pm Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached at (703) 308-4028.

Official fax numbers for this Art Unit are: (703) 308-4242, (703) 872-9306. An *unofficial* fax number, direct to the Examiner is (703) 746 5279. Please call prior to use of this number.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the TC1600 Receptionist whose telephone number is (703) 308-0196.

mkz
3/8/02

MARY K. ZEMAN
PRIMARY EXAMINER
AU 1631